

How long to wait for an antidepressant to 'work'

Ronald Pies, MD

Several recent studies demonstrate a real, drug-based response in many patients as early as the first week of treatment

Prevailing wisdom says it takes 3 to 4 weeks for an antidepressant to show clinical effect. Historically, patients who improve in the first 2 weeks have been labeled "placebo responders."¹ Several recent studies, however, demonstrate a real, drug-based response in many patients as early as the first week of treatment, depending on the medication (*Table*).^{2,5} In practical terms, these studies raise the question of how long you should wait for an antidepressant to "work."

Early indications. Here are some tips for gauging antidepressant response, depending on what you see in the first 2 to 4 weeks:

- Obtain a pretreatment score on the Beck Depression Inventory or other depression rating scale, and repeat the assessment at least once between days 7 and 10 of treatment. If there is little or no improvement, consider a modest dosage increase.
- Don't assume that a patient who responds to an antidepressant during the first 2 weeks is experiencing a placebo effect. It may be a drug-mediated response. Some patients will retain and build on this early response, whereas others' response may wane over subsequent weeks.
- No response to an antidepressant during weeks 1 through 4 does not bode well for most patients,^{5,6} although the data do not support giving up on an antidepressant after 1 to 2 weeks of nonresponse. Responses will "accumulate" during weeks 3 to 5 of treatment.⁷
- Patients who show little response during the first 2 weeks of treatment but experience some improvement during weeks 3 and 4 may be late responders. However, if

Table

Variables in antidepressant response

It is not surprising that onset of antidepressant response in some patients varies. The new data—derived mainly from meta-analyses of studies using the Hamilton Depression Rating Scale (HAM-D)—do not tease out sources of variability in the studies, including:

- heterogeneity within the construct of 'major depressive episode'
- limitations of the HAM-D total score as a measure of response
- wide variability in drug pharmacodynamics and bioavailability
- individual differences in neuronal sensitivity to antidepressants
- variability in patients' psychosocial support

the patient shows no improvement by week 3 or 4, consider switching to a different antidepressant, perhaps one from a different chemical class.⁸

- Different neurovegetative signs and symptoms of depression may improve at different rates, with some requiring >8 weeks of treatment. Insight, for example, may not improve until the second month of treatment.⁹

- Individualize treatment. Many treatment-refractory depressed patients—who failed to respond to 1 or more adequate drug trials—may require longer and more intensive treatment (>3 months) before showing a robust response.¹⁰

- "Onset of response" does not equal "clinical recovery," nor is an improved

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Hamilton Depression Scale score a proxy for “high quality of life.” Patients may need ≥ 2 months for clinically significant improvement in interpersonal, social, and vocational function.¹¹

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Acknowledgement

The author expresses his appreciation to Michael Posternak, MD, Andrew Nierenberg, MD, and Alex J. Mitchell, MD, for their helpful comments on an early draft of this article.

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